

REMARKS

Claims 1-31 are pending and have been rejected. Claims 32 and 33 have been added. Claims 1-33 remain in the case.

Claims 1-31 are rejected under the judicially-created doctrine of obviousness-type double patenting based on U.S. 5,599,712. Applicant is forwarding with this response a terminal disclaimer to obviate this rejection.

Claims 1-31 are rejected under the first paragraph of Section 112. Examiner Chen has taken the position that the specification enables administration of MnSOD, MT, or gamma-GTP to a subject locally to the targeted site, but fails to enable methods that protect "via **any administrations routes *in vivo***" (emphasis in original) More particularly, he urges that "it is unclear whether ...administration of said polynucleotide or vector to a site that is very remote from the site to be treated with irradiation can still protect cells in any targeted site in a subject *in vivo*. Applicant previously submitted evidence on this point, including

(1) ASTRO abstracts, to be presented in October 2002 in New Orleans, one of which shows that pre-irradiation intratracheal injection of MnSOD plasmid/liposomes protects mouse lungs from irradiation-induced damage.

(2) American Society of Gene Therapy Abstracts, presented in June in Boston, one of which shows protection of pulmonary endothelial cells *in vivo* from irradiation by overexpression of MnSOD.

(3) A manuscript submitted to the *Journal of Gene Therapy* showing cell phenotype specific expression of intratracheally-injected MnSOD transgene during lung radioprotective gene therapy.

(4) A manuscript submitted to *American Society of Respiratory Cellular and Molecular Biology* regarding sites of action of MnSOD plasmid liposome gene therapy in the lung, which shows that mice that received MnSOD intratracheal injections 24 hours prior to total lung irradiation demonstrated a decrease in GFP+ fibroblastic cells in the lung.

All of these results show that the present invention is protective *in vivo*.

It is not clear whether the examiner has maintained a rejection of the scope of the polynucleotide vectors. No specific comments relating to the scope of the polynucleotide vector have been made, and it is assumed that the examiner has found persuasive the evidence submitted to date on this point. In any event, applicants now forward additional evidence on each of this point, in the form of an abstract submitted to the American Society of Gene Therapy Meeting by Julie Goff and collaborators, showing HSV/MnSOD expression in human hematopoietic cells. The abstract demonstrates another vector for polynucleotide delivery.

The presently submitted evidence, along with the evidence submitted with applicant's RCE, and data previously presented in Rule 132 declarations by Dr. Joel Greenberger and Dr. Michael Lotze, clearly support applicant's presumptively accurate disclosure that the present invention is supported across the full scope of that which is claimed. Reconsideration of the rejection under Section 112 is requested.

Claims 27 and 28 are rejected under Section 102(e) based on Morrow (U.S. 5,334,383). As noted by the examiner, Morrow teaches administration of moderating and/or neutralizing amounts of *antioxidants or reducing agents*, such as superoxide dismutase or glutathione peroxidase, along with an electrolyzed saline solution to a subject, where the antioxidants or reducing agents remove superoxides, peroxides and hydroxides produced by respiratory bursts in cells. Based on this disclosure, the examiner urges that Morrow anticipates claims 27 and 28. Claims 27 and 28 do not recite compositions that contain antioxidants or reducing agents. Rather, they claim compositions that contains a *polynucleotide* that encodes a protein capable of neutralizing or eliminating a free radical, a superoxide anion, or a heavy metal cation. No possible anticipation exists.

In view of the foregoing amendments and remarks, it is believed that all claims are in condition for allowance. Reconsideration of all rejections and a notice of allowance are respectfully requested. Should there be any questions regarding this application, the examiner is invited to contact the undersigned attorney at the phone number listed below.

Respectfully submitted,

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